

CLINICAL CORRELATION

42. EPILEPSY

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A LICENSE TO DRIVE

Chief Complaint

“How long do I gotta take this stuff?”

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HPI

Joe Martinez is a 15 yo boy brought to the clinic for a routine visit by his mother. He currently has a seizure every 2 to 4 months. His seizures are described as partial complex with secondary generalization.

PMH

Birth followed a normal pregnancy and was associated with a full- term vaginal delivery. Normal developmental milestones. Developed meningitis at age 3, with onset of seizures at that time. Has been on multiple anticonvulsants over the years, but old records are sketchy at best.

FH

Negative for seizures; has two healthy siblings.

SH

Attends public school, is working one grade below his age level. Making C's

Meds

Phenobarbital 60 mg po BID

Carbamazepine 600mg po QID

ALL

Phenytoin (rash)

ROS

Negative

PE**GEN**

Exam reveals slightly obese 15 yo, Tanner stage 4 male

VS

BP 110/70, P64, RR12,T37.1C; HT 170 cm,wt 68 kg

Neuro

CNII-XII intact, reflexes normal. The remainder of the of the PE was non-contributory.

EEG

Abnormal, with left temporal lobe spikes and mild background slowing

Labs

Sodium 133mEq/L, potassium 4.6mEq/L, chloride 107 mEq/L, CO2 content 26 mEq/L, BUN 13 mg/dl,serum creatinine 0.9 mg/dl,glucose 94mg/dl, calcium 10.3 mg/dl,phosphorus 3.8 mg/dl,uric acid 4.9 mg/dl Total bilirubin 0.8 mg/dl, alkaline phosphatase 310 IU/L,GGT 42 IU/L, AST 53 IU/L,ALT 45 IU/L, protein 7.6g/dl,cholesterol 198 mg/dL.Hemoglobin 14.0 g/dL, hematocrit 43.5%, platelets 298,00/mm3, WBC 3800/mm3Carbamazepine 11.3 mcg/mL phenobarbital 17 mcg/mL.

Joe is interviewed further to determine why he does not want to take his medications. He complains that the medication makes him feel “slowed down” and “fuzzy.” He also does not think the medications are working well enough, since he still has seizures . He expresses concern that he will not be allowed to get his driver’s license next year. (NOTE : Laws vary from state to state; in Texas, a person must be seizure- free from one year to obtain a driver’s license or to have the license reinstated.)

“Epilepsy is an illness of various shapes and horrible.” – Arataeus

Epilepsy is a common neurologic disorder. Epilepsy is the third most common neurologic disorder, following stroke and Alzheimers disease. Epilepsy by definition is a condition in which individual is predisposed to recurrent seizures of a central nervous system (CSN) disorder. A seizure is a sudden, involuntary, time limited alteration in behavior including a change in motor activity, in autonomic function, is consciousness, or in sensation accompanied by abnormal electrical discharge in the brain Leppik, (1997) Patient With Epilepsy. 3rd. Edition.

1a. Does this patient's seizure history meet the definition of epilepsy?

a. Yes. Epilepsy implies a periodic recurrence of seizures with or without convulsions. A seizure results from an exesive synchronous discharge of cortical neurons and is characterized by changes in electrical activity as measured by the electroencephalogram (EEG).

Joe Martinez is a 15 yo who has recurrent seizures every 2 to 4 months. His seizures are described as partial complex with secondary generalization. Electroencephalogram abnormal with left temporal lobe spikes and mild background slowing.

b. Describe the presentation of a partial complex seizure with secondary generalization.

What are the implications for treatment compared with generalized seizures?

Partial complex seizure is a focal seizure. It may manifest as a motor movement or abnormal sensory or somatosensory symptoms or automatism. If there is loss of consciousness, they are termed complex partial and the patient may have automatism, memory loss, or aberrations of behavior.

Secondary generalization is a seizure that starts as a focal seizure and then progresses to a generalized tonic clonic seizures. The individual is about to move in a relatively normal manner but at the same time, suddenly lacking in understanding is called automatism. Common examples of automatism are lip smacking, chewing, facial grimacing, swallowing movements, and patting, picking, or rubbing oneself or one's clothing.

Temporal lobe seizures generally last 11 sec to 8 min (average 2 min). Secondary generalization is a seizure that starts as a focal seizure and then progresses to a generalized seizure. Implication for treatment compared with generalized seizures, seems that generalized seizures are more difficult to treat due to the need of higher concentration of drugs needed for treatment.

Desired Outcome

2. What are the goals of therapy for this patient?

The goal of therapy is to eliminate the seizures and ensure compliance ,allowing the patient to live as normal a life as possible and to be able to drive.

Complete suppression of seizures must be balanced against tolerability of side effects, and the patient should be involved in defining the balance.

Eliminate phenobarbital to decrease daytime sedation and improve school performance because it has been proven that phenobarbital affects the ability to learn.

<http://www.efa.org/education/meds/pheno.html>

Therapeutic Alternatives

3.What are the therapeutic alternatives available for this patient ?

Therapeutic alternatives for this patient depends on the type of epilepsy and the drug specific adverse effect and patient preference.

The alternative drugs of treatment for partial complex seizure with secondary generalization are:

CARBAMAZEPINE

Carbamazepine (tegretol) is effective alone or with other AEDs in partial seizures,especially complex partial seizures, in generalized tonic clonic seizures, and in combinations of these seizure types.The patient is not a good candidate to be in monotherapy due to quality of seizures.Serum Carbamazepine levels should be monitor closely due to high serum concentrations in this patient. Carbamazepine also has an effect in lab values, ^ BUN, AST,ALT,bilirubin, alkaline phosphatase, decrease calcium, T3,T4,sodium.

All these should also be monitor closely because these AEDs have been associated with hepatic failure. ALK phosphatase in this patient is above normal “panic” values. Therefore closely monitor of liver fuction must be performed during treatment. Should be monitor weekly. Carbamazepine may induce mild to moderate hyponatremia with sodium levels of 130mEq/l. Patient already presenting sodium levels in 133 mEq/l. Aplastic anemia and agranulocytosis are the most severe hematologic effect. CBC should be monitor quaterly or with the appearance of signs or symptoms of bone marrow depression.

GAPAPENTIN

Gabapentin (Neurontin) It is approved as adjunctive therapy for partial seizures with or without secondary generalization in adults. Is a reasonable choice for treatment for this patient because it has no significant drug interaction and there is no need for adjustment in carbamazepine treatment dose. In clinical practice, blood levels of 2 to 20 mg/L have been found to be effective. These patients are most likely to be on many other drugs, and gabapentin may be the best tolerated and least problematic.

There have been no changes in the hematologic and biochemical parameters. Unlike the other antiepileptic medications, gabapentin is not metabolized in the liver. It is almost completely eliminated by renal excretion . Thus, it does not affect the concentrations of the other antiepileptic drug.

LAMOTRIGINE

Lamotrigine (Lamictal) is approved as adjunctive therapy in adults with partial epilepsy refractory to other agents. It has been used as monotherapy and appears to be effective against many generalized seizure type in children. Lamotrigine does not appear to affect the concentration of other antiepileptic drugs. Reasonable choice for this patient but we have to consider that Carbamazepine may increase metabolic clearance of lamotrigine resulting in a decrease or shortened term of effectiveness.

Clinical experience has shown that serum concentrations between 2.0 and 20.0mg/L have been effective and tolerated. Most common adverse reaction is ataxia, dizziness, drowsiness, headaches. Rash and Steven Johnson syndrome has been observed in patients receiving concomitant valproic acid.

Dose :initial :50-100mg/day then titrate to daily maintenance dose of 100-400mg/day in 1-2 divided daily doses.

PHENOBARBITAL

Phenobarbital (Luminal) Is the drug of choice for neonatal seizures and is useful in patients with partial seizures. Phenobarbital impairs cognitive performance, can usually be dosed once daily and at bed time dosing may minimize daytime sedation. The most common side effect are fatigue, drowsiness, and depression. It's not a reasonable choice of treatment for this patient. The patient is working one grade below his age level. It has been proved that phenobarbital affects cognitive performance.

One of the adverse effects is the “hangover” effect
dizziness, clumsiness or unsteadiness, drowsiness. This
medication is not contributing to the improvement of the
patient seizure condition

Valproic Acid

Is the drug of choice for most generalized seizures and
is also useful for most generalized seizures and is also
useful for partial seizures. It may not be a drug of choice
due to decrease effect when used with carbamazepine,
phenobarbital, primidone and phenytoin. Also is not a
good choice due to hepatotoxicity. Also one of the side
effect is weight gain and the patient is actually over
weight. Other hematologic toxicities include leukopenia
with transient neutropenia and bone marrow changes.
The recommended initial dose is 15mg/kg/day. Maximum
dose is 60mg/kg/day and is useful in patients with
partial seizures.

FELBAMATE

It is approved for use in patients 14 years and older as
monotherapy and adjunctive therapy for partial seizures
with or without secondary generalization. Because of the
reports of aplastic anemia (1/3000 patients) and acute liver
failure (1/10,000 patients), it is now recommended for
patients refractory to other AEDs. It is not recommended
due to interaction with carbamazepine, may decrease
carbamazepine levels.

This medication frequently side effects are anorexia, insomnia, nausea and headache. Avoid use in patients with pre-existing liver pathology. Side effects include gastrointestinal complaints, weight gain, drowsiness, ataxia and tremor. Thrombocytopenia is common, but is responsive to a decrease in dose. Other hematologic toxicities include leukopenia with transient neutropenia and bone marrow changes.

Optimal Plan

4. Pharmaceutical care plan for this patient

Gabapentin: First we would start by adding Gabapentin 300mg at bedtime and increased to 300mg twice daily on the second day and 300mg three times daily on the third day. The manufacturer recommends doses up to 2400 or 3600mg/d. It is eliminated by renal mechanism and dosage adjustment are necessary in patients with impaired renal function. One week from starting gabapentin we can start tapering down the phenobarbital decreasing the dose to 90mg q pm x 2 weeks then 60 mg q pm x 2 weeks, then 30 mg q pm x 2 weeks and then stop.

LAMOTRIGINE

First we would start by adding lamotrigine, should be started at a dose of 50mg/d for two weeks and then increased to 100mg /d for two weeks. Then the dose can be titrated to 100mg/d. After four weeks we can start tapering down the phenobarbital to 90mg q pm x 2 weeks, then 30mg q pm x two weeks, then 30mg q pm x two weeks and then stop.

AssesmentParameters

5. How should therapy be monitored Prior to initiation of any antiepileptic medication the following laboratory studies should be done:

cbc
chemistry profile
liver function test,liver enzymes
eeg

Recommendations for Monitoring laboratory parameters when using AEDs

Carbamazepine
Cbc
Lft
Platelets
Reticulocyte count
Iron levels

If the patient in the course of treatment exhibits low or decrease white blood cell or platelet counts the patient should be monitored closely due to risk of aplastic anemia

GABAPENTIN: NO specific recommendations
Serum levels of concurrent anticonvulsants
LAMOTRIGEN: NO specific recommendations
VALPROATE: Liver function test prior to therapy and at frequent intervals.
FELBAMATE: Frequent cbcs (due to bone marrow suppression)

Patient should keep a log book where he should be asked to record severity and frequency of seizures in a seizure diary with a calendar. A record of side effect should be kept along with the exact day and time of the event.

Patient Counseling

6. What information should be provided to the patient and his mother.

Understanding the disorder and the prescribed medication by both the patient and family is of the utmost importance non-adherence to the medication regime has been identified as the single most common reason for treatment failure.

Teach patient regarding dosing, actions and drug interactions of the particular AED that is been prescribed.

Gabapentin

Take exactly as prescribed (do not increase dose or frequency or discontinue without consulting prescriber)

- One capsule on day 1 (at bed time to minimize sedation) then
- One capsule twice daily on day 2 and then
- One capsule three times daily on day 3

Then one week after starting the Gabapentin we are going to start decreasing the dose of phenobarbital until stop.

90mg at night for two weeks then,

60mg at night for two weeks then

30 mg at night for two weeks then stop.

Patient information/Instruction

Take exactly as directed (do not increase dose or frequency or discontinue without consulting prescriber)

While using this medication, do not use alcohol and other prescription or OTC medications (especially pain medications, sedatives, antihistamines, or hypnotics) without consulting prescriber. Maintain adequate hydration (2-3L/day of fluids unless instructed to restrict fluid intake). You may experience drowsiness, dizziness, or blurred vision; nausea, vomiting, loss of appetite, or dry mouth (small frequent meals may help). Wear identification of epileptic status. Report CNS changes, mentation changes, or changes in cognition; muscle cramping, weakness, tremors, changes in gait; persistent GI symptoms; difficulty breathing; changes in urinary pattern, worsening of seizure activity, or loss of seizure control.

LAMOTRIGINE

50mg at night for two weeks then,
50 mg twice daily for two weeks then

Four weeks after starting Lamotrigine we are going to
start decreasing the dose of phenobarbital until stop.

Start with taking 90 mg at night for two weeks then,
60mg at night for two weeks then,
30 mg at night for two weeks then stop.

Patient information/Instruction

Take exactly as directed(do not increase dose or frequency
or discontinue without consulting prescriber) While using
this medication, do not use alcohol and other prescription or
OTC medications without consulting prescriber.Maintain
adequate hydration(2-3 l/day of fluids unless instructed to
restrict fluid intake).You may experience drowsiness,
dizziness, or blurred vision,nausea,vomiting,loss of
appetite,heartburn,or dry mouth.(small frequent meals may
help)Wear identification of epileptic status and
medicationsReport CNS changes,mentation changes or
changes in cognition;persistent GI symptoms;skin
rash;swelling of face,lips or tongue;easy bruising or
bleeding;vision changes;worsening of seizure activity,or loss
of seizure control.

Driving and regulatory issues

Each state has its own regulations regarding relicensing.
Here in Puerto Rico there is not set a seizure – free period
and there is no periodic medical updates required.

Of all the limitations placed on a person with epilepsy,
loss of a driving privilege may be the most serious . Not
being permitted to drive drastically alters a person's
mobility and suddenly puts him or her in a dependant role.
This loss may be particularly devastating to active,
independent persons living in areas lacking adequate public
transportation. One patient confessed that the diagnosis of
having a brain tumor was not nearly as devastating as losing
driving privileges.

“Let’s talk about...”

SEIZURES

What is it? A seizure (c-zure) is also called a convulsion. It is a sudden attack of brain activity that causes you to lose control of your actions. You may have jerking of your face, arms or legs. There are many different kinds of seizures. Seizures may last seconds or minutes and can happen to people of any age.

Causes: The most common cause of seizures is Idiopathic epilepsy. This means that the cause of epilepsy is not known. It is a brain disease that may cause you to have more than one seizure.

Signs/symptoms: You may have a warning that you are going to have a seizure. When a seizure starts, you may pass out. You may not be aware that your face or body is jerking. You may urinate or have a BM. Without knowing it. Or you may throw up. After the seizure, you may feel irritable, confused or sleepy.

Care: You may need medication to keep from having more seizures. Teach the people around you what to do if you have a seizure. Wear a medical ID. Bracelet that will tell others that you have seizures.

Care Agreement: Discuss your treatment options with your care giver. You can work with him/her to decide what medicine and care will be used to treat your illness. You always have the right to refuse treatment.

GENERAL INFORMATION:

A seizure, or Convulsion is uncontrolled jerking of the arms, legs or face that lasts anywhere from a few seconds to several minutes. Seizures can occur after a head injury, stroke, or brain tissue infection. In more than half of patients the cause is not known.

INSTRUCTIONS FOR YOU:

Your provider has prescribed medicine to prevent seizures. Take exactly as directed. Do not stop taking the medicine without talking to your provider first. Avoid activities in which a seizure would cause danger to yourself or to others. Do not operate dangerous machinery, swim alone or climb in high or dangerous places such as ladders, roofs or girders. Do not drive until your provider says you may. Wear an emergency medical identification bracelet with information about your seizures. If you have a seizure, people around you will know what is wrong and get appropriate help. If you have any warning that you may have a seizure, lie down in a safe place where you can't hurt yourself. Teach your family and close friends what to do if you have a seizure.

Instructions for others if a seizure occurs:

Stay Calm, keep the person from falling onto harmful objects. Move hard or sharp objects out of the way. Don't force anything in to the person's mouth or try to open clenched jaws. Turn the person on his or her side when the violent movement stops or if she or he is vomiting. When the seizure is over, the person may be confused or drowsy. Reassure the person that he/she is all right. Help him/her to rest and relax.

CALL IF: You have any problems that might be related to the medicine you are taking. If a seizure occurs and:
The person doesn't wake shortly after the seizure.
The person has new problems (such as difficulty seeing, speaking or moving).

RETURN IMMEDIATELY IF:

If a seizure occurs and:

*The person was injured during the seizure.

*The person has a temperature over ____F ____C
or vomited and breathed the vomit into his or her
windpipe.

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